Diagnostic Value of Finger-guided Prostate Nodule Biopsy Combined With Systemic Random Biopsy

I-Ni Chiang,1,2 Shang-Jen Chang,3 Yeong-Shiau Pu,1,2 Kuo-How Huang,1,2 Hong-Jen Yu,1,2 Chao-Yuan Huang1,2*

Background/Purpose: The purpose of this study was to compare prostate cancer detection rates and pathology results, using the Gleason grading system, of 12-core systemic random transrectal ultrasound-guided prostate biopsy (SB) and 3-core finger-guided prostate nodule biopsy (FGNB).

Methods: Between January 2002 and December 2006, 148 patients with digitally palpable prostate nodules received SB and additional FGNB. The prostate cancer detection rates and Gleason scores of positive cancer specimens were compared between SB and combination biopsy (SB + FGNB). The patients’ characteristics, including age, prostate specific antigen (PSA), percentage of free PSA and prostate volume were also recorded.

Results: With simple SB, FGNB, and combination biopsy, the prostate cancer detection rates were 39.9%, 37.9%, and 44.6%, respectively. Of the 66 patients with prostate cancer, the Gleason sum was underestimated in three patients with simple SB only and in one patient with FGNB only. The false-negative rates for SB and FGNB were 10.6% and 15.2%, respectively.

Conclusion: In patients with a palpable prostate nodule, combination biopsy with systemic and nodule biopsy could avoid some misdiagnoses of prostate cancer and provide more accurate information for pathology grading. [J Formos Med Assoc 2009;108(9):713–718]

Key Words: biopsy, diagnostic techniques and procedures, pathology, prostate cancer

Digital rectal examination (DRE) is an established and important part of a patient’s physical examination by both urologists and general physicians in evaluating prostate and rectal problems. With the use of systemic random prostate biopsy and the development of prostate specific antigen (PSA) testing, the importance of DRE is no longer emphasized as much as before in detection of prostate cancer. In determining histological progression of prostate lesions, transrectal ultrasound (TRUS) is an advance over traditional purely digital guided biopsy. TRUS provides real-time monitoring of biopsy tracts and random sampling of the prostate lesions that cannot be visualized and that are nonpalpable.1 In 1989, Hodge et al originally proposed the concept of random systemic sextant prostate biopsy, which minimizes observer and sampling errors with lesion-directed biopsy.2 Later, several studies found an improvement in prostate cancer detection with extended-core TRUS-guided prostate biopsy protocols. Initially, 10- to 12-core prostate biopsies were suggested by most investigators.3 Recently, some studies have even recommended a 21-core prostate

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biopsy protocol to provide early diagnostic and prognostic value in patients with prostate cancer.4 However, it has been questioned whether systemic random prostate biopsy without lesion-guided sampling was sufficient for all patients suspected of having prostate cancer. Some studies have documented the importance of additional lesion-guided biopsies with positive ultrasound findings or positive DRE.5–7 In this article, the 12-core systemic biopsy together with a 3-core finger-guided nodule biopsy (FGNB) is defined as combination biopsy. This study aimed to present a retrospective analysis of combination biopsy to survey whether the proposed strategy would yield a higher prostate cancer detection rate.

**Methods**

Between January 2002 and December 2006, 148 patients with digitally palpable prostate nodules underwent systemic random 12-core TRUS-guided prostate biopsy (SB) with additional 3-core FGNB at the National Taiwan University Hospital. The indication for biopsy was a positive DRE diagnosis noted by a single physician. All patients gave their informed consent.

Rectal preparation with bisacodyl was performed 6 hours before biopsy. Patients taking antiplatelet/anticoagulation agents were instructed to discontinue aspirin 7 days before biopsy and to discontinue warfarin 3 days before biopsy. Between January 2002 and December 2004, patients received pipemidic acid 500 mg twice daily for 3 days starting from the day of biopsy. In the period from January 2005 to December 2006, patients received a single dose of levofloxacin (500 mg) in the morning before biopsy.

TRUS examinations were performed with a real-time ultrasound scanner (Model 1846; Brüel & Kjær Sound & Vibration Measurement A/S, Nærum, Denmark) using a 7-MHz transducer. Prostate volume was calculated from the TRUS image using the formula: volume (cm$^3$) = 0.52 × length × width × height (cm). Patients were placed in the left decubitus position. Biopsies were done with 18G tru-cut biopsy needles during longitudinal scanning.

Concerning the sequence, FGNB was performed first. Each nodule biopsy included three biopsy cores. Then, SB, standard sextant biopsy with an extra three cores taken from each side of the more lateral prostate areas, including the base, midlobe, and apex was performed. The combination biopsy left lateral (LL), left medial (LM), right medial (RM), right lateral (RL), and nodule specimens were placed in five respectively labeled containers. All specimens were fixed in formalin and evaluated according to the Gleason grading system. Prostate cancer detection rates and Gleason scores of positive cancer specimens were compared between SB, FGNB, and combination biopsy (SB + FGNB). The patients’ characteristics, including age, PSA, percentage of free PSA and prostate volume were also recorded.

Data were analyzed using MedCalc version 9.3.0.0 (MedCalc Software, Mariakerke, Belgium) for Windows. The $\chi^2$ test was used to compare categorical variables. Dependent continuous variables were analyzed with ANOVA and the paired t test. For all tests, a $p$ value $<$ 0.05 was regarded as significant.

**Results**

Of the 148 patients, 66 (44.6%) patients had prostate cancer detected. The prostate cancer detection rates for SB, FGNB, and combination biopsy were 39.9%, 37.9%, and 44.6%, respectively. Positive pathology findings for 49 patients were detected in both SB and FGNB specimens. Positive pathology findings were detected in the FGNB specimens of only seven patients, and in the SB specimens of only 10 patients. Although combination biopsy yielded a higher overall prostate detection rate than FGNB ($p = 0.410$) and SB ($p = 0.238$) alone, the difference was not statistically significant. The clinical characteristics including age, prostate volume, PSA, and percentage of free PSA were not significantly different between patients with prostate cancer diagnosed by
FGNB alone, by SB alone, or by combination biopsy (Table 1). Of the 148 patients, 63 (42.6%) patients were noted to have suspicious prostate hypoechoic lesions on TRUS. There was no statistically significant difference in prostate detection rates between patients with and without TRUS findings, 36.5% versus 50.6% ($p = 0.088$).

The pathology results of both SB and FGNB specimens from patients with prostate adenocarcinoma according to the Gleason grading system were analyzed. Overall, there were 66 patients with prostate cancer. In the combination biopsy specimens, each of the three cores of prostate tissue from the five different portions of the prostate was defined as a single specimen. Overall, 203 specimens had prostate adenocarcinoma detected out of 330 specimens from 66 men with prostate cancer. Of these, 147 specimens with cancer were obtained from SB, and 56 specimens with cancer were obtained from FGNB. The positive rates of specimens obtained from FGNB and SB were considered as an index of the sensitivity of these two biopsy methods. In this study, for the patients with prostate cancer, the positive pathology rate of FGNB specimens was significantly higher than the positive pathology rate of SB specimens (84.8% vs. 54.7%; $p < 0.001$). Mean Gleason scores, which were 7.25 ± 1.13 and 7.21 ± 1.04 for FGNB and SB respectively, showed no significant difference ($p = 0.858$). Overall, the proportion of Gleason sum ≥7 accounted for 80.3% of the patients with prostate cancer. The specimens obtained from FGNB had a higher proportion of Gleason sums ≥7 in comparison with SB (83.9% vs. 76.7%; $p = 0.262$). The Gleason sum was underestimated in three patients with SB alone and in one patient with FGNB alone. As for clinical staging, 47 (71.2%) patients were T2, 15 (22.6%) patients were T3, and four (6.2%) patients were T4. Eleven (16.7%) patients were noted to have distant metastasis. They had a significantly higher Gleason sum (8.00 vs. 7.04; $p = 0.004$) and higher serum PSA (105.8 ng/mL vs. 19.1 ng/mL; $p < 0.001$).

Prostate cancer was detected in both SB and FGNB specimens.

There was no significant difference in positive pathology rates and Gleason scores of specimens from the LL, LM, RM and RL aspects of the prostate. The lateral portions of the prostate did not yield significantly higher positive biopsy rates than the medial portions (56.8% vs. 54.5%; $p = 0.711$) (Table 2). In our study, SB specimens were divided into the ipsilateral side and contralateral side of the palpable nodule. SB specimens from the ipsilateral side of the prostate nodule had a significantly higher positive pathology rate than did specimens from the contralateral side (67.4% vs. 43.1%; $p = 0.001$).

To evaluate the safety of the 15-core combination biopsy, we also recorded any major complications after biopsy, defined as complications requiring readmission or an emergency room visit. Of the 148 patients, nine (6.1%) experienced major postoperative complications, including fever, acute urinary retention, and gross hematuria.

**Discussion**

In our study, the prostate cancer detection rates, diagnostic value, and safety of combination biopsy

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**Table 1.** Comparison of clinical characteristics of patients with prostate cancer detected by nodule biopsy alone (N), systemic biopsy alone (S), and both nodule and systemic biopsy (N+S)

<table>
<thead>
<tr>
<th></th>
<th>N (n = 7)</th>
<th>S (n = 10)</th>
<th>N + S (n = 49)</th>
<th>Total (n = 66)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>74.14 ± 4.56</td>
<td>71.50 ± 11.23</td>
<td>69.96 ± 7.71</td>
<td>70.64 ± 8.07</td>
<td>0.417</td>
</tr>
<tr>
<td>Prostate volume (mL)</td>
<td>35.07 ± 15.34</td>
<td>35.57 ± 3.35</td>
<td>41.05 ± 22.93</td>
<td>39.82 ± 20.24</td>
<td>0.886</td>
</tr>
<tr>
<td>PSA (ng/mL)</td>
<td>26.71 ± 28.14</td>
<td>11.91 ± 4.84</td>
<td>39.68 ± 84.34</td>
<td>34.27 ± 73.88</td>
<td>0.570</td>
</tr>
<tr>
<td>Free PSA (%)</td>
<td>3.50 ± 2.88</td>
<td>9.67 ± 9.27</td>
<td>9.40 ± 8.52</td>
<td>8.83 ± 8.25</td>
<td>0.359</td>
</tr>
</tbody>
</table>

PSA = prostate specific antigen.
with SB and FGNB were evaluated. It was found that additional FGNB improved the prostate cancer detection rate by 4.7%. Reducing the false-negative rate of prostate biopsy will avoid repeat biopsy and optimize early detection and treatment planning for patients with prostate cancer.

DRE is suggested for men older than 40 years old and for men of any age who have genitourinary symptoms. It is probably the most common physical examination in the urological clinic, but it may be the most unpleasant part of a physical examination because of patients’ embarrassment and discomfort. DRE is utilized in the detection of prostate and rectal diseases, including benign prostate hyperplasia, acute prostatitis, prostate cancer, hemorrhoids, rectal cancer, rectal polyps, anal fistula and fissures.8 With the development of PSA measurement, TRUS, computed tomography, and endorectal magnetic resonance imaging,9 there are many novel tools for prostate cancer detection. There have been studies discussing the role of DRE in the early detection of prostate cancer. Schroder et al claimed that for patients with low PSA values (0–3.9 ng/mL), the positive-predictive value and sensitivity of DRE, tumor volume, and tumor grade are strongly dependent on PSA level, and that DRE does not perform well.8 Philip et al reviewed 12-core prostate biopsy results, DREs and the pathology presentations of radical prostatectomy specimens from 408 patients with PSA of 2.5–10 ng/mL.10 They found that the prostate cancer detection rates were 47% in patients with abnormal DRE (which is similar to our findings) and 27% in patients with normal DRE, but almost 40% of the patients with prostate cancer stage T2 to T4 had a normal DRE.

In our study, it was found that 44.6% of 148 patients with palpable nodules were diagnosed with prostate cancer. In our previous study, the prostate cancer detection rate in 1875 patients with elevated PSA, with or without palpable nodules, was 28.5%.11 There have also been some studies recognizing the diagnostic value of DRE. In 1987, Guinan et al compared five tests used in the diagnosis of prostate cancer which, in decreasing order of accuracy, were DRE, PSA, TRUS, acid phosphatase and, finally, aspiration cytology.12 Sheikh et al conducted a study to determine the usefulness of DRE, TRUS and serum PSA in the diagnosis of prostate cancer in Arab men.13 They found that DRE(+) tripled the probability of cancer detection, while TRUS was only significantly associated with detection of cancer if PSA was elevated. Roobol et al evaluated the value of screening tests in identifying men with an elevated risk of having prostate cancer and the differences between three centers in the European Randomised study of Screening for Prostate Cancer (ERSPC) with 2483 patients, and found that the predictive values of DRE and TRUS varied considerably among the three centers.14 In Australia, Huynh et al found that FGNB, in addition to SB, in patients with palpable prostate nodules could increase the prostate cancer detection

### Table 2. Comparisons of positive pathology rates and Gleason scores between specimens from different prostate portions: left lateral (LL), right lateral (RL), left medial (LM), right medial (RM), and nodule (N)

<table>
<thead>
<tr>
<th>Specimens (n)</th>
<th>LL</th>
<th>RL</th>
<th>LM</th>
<th>RM</th>
<th>N</th>
<th>Total</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive rate (%)</td>
<td>57.6</td>
<td>56.1</td>
<td>53.0</td>
<td>56.1</td>
<td>84.8</td>
<td>61.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gleason score</td>
<td>7.17±0.96</td>
<td>7.19±0.85</td>
<td>7.17±0.19</td>
<td>7.32±1.08</td>
<td>7.25±1.13</td>
<td>7.22±1.06</td>
<td>0.972</td>
</tr>
<tr>
<td>Positive rate (%)</td>
<td>56.8</td>
<td>54.5</td>
<td>84.8</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gleason score</td>
<td>7.18±0.95</td>
<td>7.25±1.13</td>
<td>7.25±1.13</td>
<td></td>
<td></td>
<td></td>
<td>0.917</td>
</tr>
<tr>
<td>Positive rate (%)</td>
<td>55.7</td>
<td></td>
<td>84.8</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gleason score</td>
<td>7.21±1.04</td>
<td>7.25±1.13</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.858</td>
</tr>
</tbody>
</table>
rate from 47.9% to 55.4%. Furthermore, Mancuso et al demonstrated that, of 500 men with a palpable prostate nodule over 6 years, 14.6% were diagnosed with prostate cancer using FGNB only. In our study, FGNB increased the prostate detection rate from 39.9% to 44.6%.

DRE techniques are explained in detail in most textbooks in the fields of physical examination and urology, as Marshall described. In our study, the insertion of an adequately lubricated, slow, steady, slightly-circling single digit, as well as an explanation of the possible voiding or defecation desires can decrease patient discomfort. As for the technique of FGNB, the importance of the biopsy sequence has to be strongly emphasized. FGNB should be performed before SB. If SB is performed first, swollen prostate tissue will mask the digital sensation of the prostate nodule.

In our study, a trumpet-like biopsy guide device was used for FGNB, as in the procedure described by Woo et al. For the physicians' safety, the fingers should always be kept behind the tip of the biopsy guide.

In the early 1990s, there were several studies comparing the diagnostic values of ultrasound-guided and traditional digital-guided prostate biopsy. Van Every and Rooney found that the two methods were comparable in terms of prostate cancer detection. In Türkeri et al's study of 40 patients with palpable prostate nodules, they compared the efficacy of digital- and ultrasound-guided prostate biopsies, and found 10 patients with normal TRUS findings. Systemic biopsy revealed 21 patients with prostate cancer, while digitally-guided prostate biopsy yielded only 18 patients with prostate cancer. The authors concluded that systemic biopsies are necessary regardless of TRUS findings, and that digitally-guided biopsies are unnecessary. Lan et al discussed the controversial issue of lesion-guided biopsy by evaluating the diagnostic performance of random versus lesion-guided biopsy of the prostate, based on TRUS. In this study, although the cancer detection rate of lesion-directed TRUS biopsy was superior to that of random biopsy, in some cases prostate cancer was diagnosed in sonographically normal images, appearing in half of the prostates. Thus, systemic random biopsy is mandatory.

Palpable prostate nodules may present with normal TRUS images, and there are varied TRUS presentations of prostate cancer. The digitally lesion-guided prostate biopsy can compensate for the insufficiency of TRUS lesion-guided biopsy in patients with palpable nodules and normal or equivocal ultrasound images. In our study, it was found that combination biopsy can avoid some false-negatives with SB or FGNB, but FGNB specimens did not show significantly higher histology grading than SB specimens. An abnormal DRE has been shown to be an independent predictor for prostate cancer and was associated with a Gleason sum ≥ 7 in multivariate analysis. Also, it was noted that in patients with abnormal DRE, the specimens obtained from FGNB had a higher proportion of Gleason sums ≥ 7. Although the increase did not reach statistical significance, the present study could not neglect the benefits of FGNB. Without FGNB in addition to SB, the Gleason sum of three patients would have been underestimated, and seven patients would have been misdiagnosed. In our study, with simple SB and simple FGNB, the false-negative rates were 10.6% and 15.2%, respectively. It could be hypothesized that SB would detect lesions that are too small to be visualized and palpated, and FGNB would increase the cancer detection rate by avoiding misdiagnosis as a result of random sampling. In this study, conducted on 148 patients with palpable prostate nodules, combination biopsy yielded the highest cancer detection rate. Previous studies documented the clinical significance of TRUS lesion-guided prostate biopsy. In our study, no additional TRUS lesion-guided biopsy on these patients was performed because, after FGNB, the TRUS images were confusing.

As for complications following prostate biopsy, several studies have documented the safety of increasing the number of prostate biopsy cores, i.e. without increasing complications, for up to 21 cores. The major complication rate of 15-core combination biopsy in this study was 6.1%. In our
previous study on the complications of prostate biopsy, there was no significant difference in complication rates among the 6-, 12- and 15-core groups, which were 6.34%, 6.90% and 6.95%, respectively. Thus, in patients with a palpable prostate nodule, combination biopsy appears to be a safe and effective biopsy regimen.

In patients with a palpable prostate nodule, combination biopsy with systemic versus nodule biopsy avoids some misdiagnoses of prostate cancer and could provide more accurate information for pathology grading.

References